REMARKS

Entry of this Amendment and reconsideration of the subject application in view thereof are respectfully requested.

I. Claims

Claims 1-4 were pending and these claims stood rejected.

II. Rejection Under 35 U.S.C. § 103

Claims 1-4 were newly rejected under 35 U.S.C. § 103(a) as being unpatentable over Donson et al., 1994, US Patent 5,316,931("'931") in view of Ma et al., 1994, Eur. J. Immunol. 24:131-138, Goodman et al., 1990, U.S. Patent 4,956,282 and Donson et al., 1991, PNAS 88:7204-7208.

Applicant respectfully disagrees with and traverses the assertions made in the Office Action and the rejection premised thereon.

A determination of obviousness must involve more than an indiscriminate combination of the prior art; there must be some motivation, suggestion, or teaching of the desirability of combining or modifying the references to arrive at the claimed method. *In re Dance*, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998). The prior art must also have revealed that in so making or carrying out the claimed method, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Rejecting claims solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed inventions itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention is "an inappropriate process by which to determine patentability." *Sensonics, Inc. v. Aerosonic Corp.*, 38 USPQ2d 1551 (Fed. Cir. 1996). The requisite teaching or suggestion to combine the teachings of the cited prior art references is absent when one of the cited references teaches away from rather than toward the claimed features. *In re Bell*, 991 F.2d 781, 26 USPQ 2d 1529, 1532 (Fed. Cir. 1993). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be led in a direction divergent from the path

that was taken by the applicant. *In re Gurley*, 27 F.3d 551, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

A case of *prima facie* obviousness of claims 1-4 has not been made by the Examiner, and the disclosures of the cited art are deficient and there is no reasonable expectation of success based on the art of record, as further pointed out in the discussion that follows.

Donson ('931) teaches a method for systemically expressing foreign genes in plants via viral vectors. The foreign sequence can be an antibody. See, Donson ('931) at Column 14, lines 59-67. Donson employs only a single vector to express foreign genes including antibody genes. Donson does not teach or suggest two different vectors to express a protein. Specifically, as noted by the Examiner, Donson ('931) is deficient in that it does not teach a method for the production of a full-length antibody in a host plant by introducing separate vectors expressing light and heavy chains. Indeed, Donson teaches or suggests exactly the opposite. See, for example, Donson at Column 3, line 59 through line 42, where it states that:

> [t]he recombinant plant viral nucleic acid may contain one or more additional non-native subgenomic promoters. Each non-native subgenomic promoter is capable of transcribing or expressing adjacent genes or nucleic acid sequences in the plant host and incapable of recombination with each other and with native subgenomic promoters.
>
> Non-native (foreign) nucleic acid sequences may be inserted adjacent the native plant viral subgenomic promoter or the native and a non-native plant viral subgenomic promoters if more than one nucleic acid sequence is included. The non-native nucleic acid sequences are transcribed or expressed in the host plant under control of the subgenomic promoter to produce the desired products.
>
> ...The inserted non-native subgenomic promoters are capable of transcribing or expressing adjacent genes in a plant host and are incapable of recombination with each other and with native subgenomic promoters. Non-native nucleic acid sequences may be inserted adjacent the non-native subgenomic plant viral promoters such that said sequences are transcribed or expressed in the host plant under control of the subgenomic promoters to produce the desired product....
>
> ... The recombinant plant viral nucleic acid is capable of replication in the host, systemic spread in the host, and transcription or expression of foreign gene(s) in the host to produce the desired product. Such products include

> therapeutic and other useful polypeptides or proteins ... complex biomolecules ...

Thus, the Donson ('931) teachings are explicit in that the recombinant plant viral vector can be advantageously used for expressing more than one nucleic acid sequence (e.g., an antibody sequence and a ribozyme sequence on a single vector, heavy and light chain sequences of an antibody on a single vector etc.,) by inserting each sequence adjacent a subgenomic promoter in the vector. Therefore, upon reading the above teachings of Donson ('931), a person of ordinary skill in the art would use only one vector to produce a full-length antibody in a host plant rather than constructing and using two different vectors to achieve the same goal. In other words, upon reading Donson ('931) reference, a person of ordinary skill in the art would be led in a direction divergent from the path that was taken by the Applicant. Stated otherwise, the teachings of Donson ('931) reference is a *per se* demonstration of lack of *prima facie* obviousness of the claimed invention. Thus, Applicant respectfully submits that the rejection premised on the primary reference is fatally flawed.

Ma, Goodman and Donson (1991) likewise fail to remedy the deficiencies of Donson ('931) reference. In particular, as the Examiner The Examiner cites Goodman for teaching light and heavy chains and Ma for teaching the assembly of monoclonal antibodies in plants. As the Applicant has already noted and as the Examiner concedes the Ma and Goodman involve transgenic approach and this approach is directly contrary to the approach adopted by the Applicant.

The Examiner cites Donson (1991) as motivation providing reference. Specifically, the Examiner contends that one would have been motivated to use Donson's viral vectors instead of transgenics because it "teaches that viral vectors are simpler and less time-consuming than transgenics." Applicant respectfully disagrees and submits that Donson (1991) fails to as motivation providing reference for several reasons readily apparent from the cited art. For example, Donson (1991) reports on page 7207, first column that levels of extractable NPTII protein (i.e., the levels of foreign sequences produced in plants via the viral vectors) were considerably lower than levels of the viral coat protein produced in plants. Further, several years after the publication by Donson (1991) and until the Applicant's present invention, it is the transgenic approach, not the transient viral vector approach, has been shown to be possible for

high-level expression of heavy and light chains and their assembly into a full-length antibody as demonstrated by Ma. See abstract, on page 131, of Ma.

A person of ordinary skill, upon reading the Ma reference (suggesting high-level expression of complex antibodies via transgenic approach) and the Donson (1991) reference (suggesting considerably low-level expression of foreign sequences that are less complex than antibodies via transient viral vector approach) would be led in a direction divergent from transient viral vector approach taught by Donson for the production of proteins in plants. Such references may be said to teach away. The requisite teaching or suggestion to combine the teachings of the cited prior art references is absent when one of the cited references teaches away from rather than toward the claimed features. In other words, and particularly in the context of a full-length antibody production in plants, the teachings of Ma and Donson (1991) references are by themselves a demonstration of lack of *prima facie* obviousness of the claimed invention.

The Examiner also relies on Donson ('931) reference to show motivation because this reference teaches that viral vectors are advantageous over transgenics as the transformation and regeneration of target organisms are required. Even if, *arguendo*, there was some suggestion or motivation to use Donson's viral vectors, Donson (1991) fails to remedy the deficiencies of Donson ('931) reference. Specifically, Donson (1991) does not provide any teaching, suggestion or motivation to a person skilled in the art to modify Donson's ('931) teachings in order to arrive at a method for the production of a full-length antibody in a host plant by introducing separate vectors expressing light and heavy chains.

In fact, there is no evidence of record to suggest why one of skill in the relevant art would be motivated to combine references in the manner averred by the Examiner. Applicant believes that the Examiner attempts to recite a "hindsight reconstruction" of the claimed invention, which is an inappropriate process under a § 103 analysis.

Applicant also notes that none of the cited references, either alone or in combination with the other cited art, provides a proper basis for any reasonable expectation of success in achieving Applicant's invention. As pointed out above, Ma reports high-level expression of complex antibodies via transgenic approach. Donson (1991) reports low-level expression of foreign sequences that are less complex than antibodies via transient viral vector approach. Applicant also points out that the transgenic approach allows one to select cells expressing both heavy and

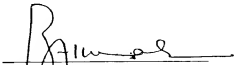
light chains and regenerate such cells into whole plants. Thus, there is a reasonable expectation of success that the heavy and light chains can be expressed and assembled into the full-length antibodies in plant cells. Ma's transgenic approach suggests nothing about how the heavy and light chains can be assembled into the full-length antibody in a plant simply by introducing heavy and light chain sequences on separate viral vectors claimed here. There is nothing in the art to suggest that one would be successful in expressing and producing a full-length antibody in a host plant using separate viral vectors. For a proper rejection under § 103, in addition to suggesting the claimed invention, the prior art must also have revealed that in so making or carrying out the claimed method, those of ordinary skill would have a reasonable expectation of success. The combination of Donson ('931) Ma, Goodman and Donson (1991) further fails to satisfy this requirement.

Accordingly, Applicant can find nothing on the record which supports a reasonable inference that the present invention is *prima facie* obvious, let alone a reasonable expectation of success on the part of one of skill in the relevant art, even if Donson ('931) is combined with Ma, Goodman and Donson (1991). Even if *prima facie* obviousness has been established, which it has not, it is urged that the cited art nonetheless fails to render the present invention obvious under a proper § 103 analysis, as the proper suggestions and motivations are lacking. If the Examiner is aware of references which would tend to remedy the shortcomings of Donson ('931), the Examiner is asked to cite them. If such facts are within the Examiner's personal knowledge, the Examiner is requested to make them part of the record by way of affidavit as required by 37 C.F.R. § 1.104(d)(2). In the absence of such additional disclosures, the rejection under § 103 is improper. Reconsideration and withdrawal of the rejection are respectfully requested.

III. Conclusion

Applicant believes this response to be a full and complete response to the Office Action. Accordingly, favorable reconsideration in view of this response and allowance of all of the pending claims are earnestly solicited. Should any matters remain that might be resolved by telephone, the Examiner is courteously invited to contact the undersigned at the number given below.

Respectfully submitted,



Date: April 21, 2003

William J. McNichol, Jr.
Registration No. 31,179
Nanda P.B.A. Kumar
Registration No. 44,853
Attorneys for Applicant

REEDSMITH LLP
2500 One Liberty Place
1650 Market Street
Philadelphia, Pennsylvania 19103-7301
Fax: (215) 241-7945
Attn: William J. McNichol, Jr., Esq.
(215 241-7950)
Nanda P.B.A. Kumar
(215 241-7991)